Medicinska istaživanja 2023; 56(2):61-68 | DOI: 10.5937/medi56-42544

OPEN ACCESS

Medical Research | Published by Faculty of Medicine University of Belgrade

ORIGINAL ARTICLE

Magnetic resonance angiography in children with arterial hypertension – a single-center experience

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Recived: 30 January 2023

Revised: 02 March 2023

Accepted: 20 April 2023

Check for updates

Funding information:
The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Competing interests:
The authors have declared that no competing interests exist

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Summary

Introduction: Renal blood vessel (RBV) stenosis is the cause of secondary arterial hypertension (AH) in 10% of children. Digital subtraction angiography (DSA) is the gold standard in diagnosing RBV stenosis. Many authors suggest MR angiography (MRA), a non-invasive method without radiation, as an adequate diagnostic method. Our aim was to analyze the experience of our center in using MRA in children with AH.

Method: This retrospective study included 148 patients hospitalized at the University Children's Hospital in Belgrade, due to AH. After initial examination, patients underwent DSA and/or MRA.

Results: According to the current guidelines, DSA was performed in patients with highly suspected RBV stenosis, and the diagnosis was confirmed in 13/29 (45%). Diagnostic MRA was done in 116/119 (97.5%) patients, and control MRA was done after therapeutic revascularization in 3/119 (2.5%). In 4/116 (3.5%) patients, the findings indicated RBV stenosis, and in 44/116 (38%) it indicated some other abnormality of the kidney parenchyma and the urinary tract or RBV varieties. After MRA, DSA was performed in 7/116 (6%) patients (4 with RBV stenosis on MRA and 3 with clinical suspicion of RBV stenosis), but all findings were normal.

Conclusion: According to the results, it is justified to perform a diagnostic MRA before DSA in children with highly suspected RBV stenosis, in order to avoid DSA which is an invasive procedure with radiation, in some patients with normal findings. Also, over time, we would have a clearer view of the sensitivity and specificity of MRA as a diagnostic method in RBV stenosis in children.

Keywords: Renal blood vessel stenosis, arterial hypertension, MR angiography, digital subtraction angiography, children

Cite this article as: Cvetković M, Miloševski-Lomić G, Petrović A, Spasojević B, Paripović D, Đukić M, Pavićević P, Gojković I, Gaus T, Radović T, Stefanović I, Kostić M. Magnetic resonance angiography in children with arterial hypertension - a single-center experience; Medicinska istaživanja 2023; 56(2):61-68; DOI: 10.5937/medi56-42544

INTRODUCTION

In children up to 16 years of age, the definition of arterial hypertension (AH) is arbitrary and implies systolic and/or diastolic blood pressure ≥ 95th percentile for sex, age and body height, and in adolescents over 16 year of age, it is an absolute value of blood pressure ≥ 140/90 mmHg, in three separate measurements (1). The prevalence of AH in children is between 2 and 4% (2). Stenosis of the renal blood vessel is the cause of secondary AH in about 10% of children and adolescents (3-6), and it is extremely important to establish the diagnosis considering therapeutic possibilities and treatment (5, 7). The causes of renovascular hypertension (RVH) in children are significantly different compared to the adult population **(Table 1)**, in which atherosclerosis is the major cause in 75-80% of cases (5). In India and South Africa, Takayasu arteritis is the most common cause of RVH in children, while in the rest of the world it is fibromuscular dysplasia (8). Clinical symptoms, signs and laboratory findings that may raise suspicion of RVH (7) are shown in **Table 2**. Digital subtraction angiography (DSA), an invasive imaging method that requires radiation, is still the gold standard in diagnosing RVH in children (9). On the other hand, among the non-invasive imaging methods, Doppler ultrasound, renal scintigraphy, CT angiography (CTA) and magnetic resonance angiography (MRA) are also available. These methods are considered, by numerous authors, as possible adequate screening methods for the diagnosis of renal blood vessel stenosis (RBV stenosis) (7, 10-13). MRA has its advantages. In addition to being a non-invasive method and requiring no radiation, it enables a detailed analysis of the kidney parenchyma. The disadvantage is that it requires sedation or anesthesia in small children, and the gadolinium-based contrast agent, is contraindicated in children with GFR<30 ml/min/1.73 m^2 (in most cases, gadolinium-based contrast agent should not be used in children with GFR<60 ml/min/1.73 m2) due to the risk of systemic fibrosis (14). There are few studies available in literature that investigated the sensitivity and specificity of MRA in children with RVH. The aim of this study was to analyze our center experience of using MRA in children with AH.

Table 1. Causes of renovascular hypertension in children.

Genetics / Syndromes
Neurofibromatosis type 1 Alagille syndrome Williams syndrome
Acquired conditions
Takayasu arteritis Kawasaki vasculitis Polyarteritis nodosa
Idiopathic renal artery stenosis
Fibromuscular dysplasia (histopahologic diagnosis)
Mid aortic syndrome
Congenital Acquired
External renal artery compression
Neuroblastoma Wilms tumor
Other
Radiation Trauma Transplant renal artery stenosis

Table 2. Signs, symptoms and laboratory findings associated with renocascular hypertension.

Extremely high blood pressure symptoms and secondary complications
Headache, convulsions, facial paralysis, stroke Left ventricular hypertrophy, heart failure
Hypertension poorly controlled with two or more antihypertensive drugs
Conditions with high risk of renovacular hypertension
Neurofibromatosis type 1 Williams syndrome
Signs and symptoms of vasculitis
Malaise High temperature Weight loss Weak pulses Skin rash Arhralgia Auscultatory abdominal murmur
Previous vascular insults
Renal artery thrombossis Umbilical artery catheterization Previous trauma or radiation
Kidney transplant
Auscultatory bruits above renal arteries
Clomerular filtration rate drop after introducing ACE inhibitors or Angiotensin receptor blockers (ARBs)
Increase of Plasma rennin activity (PRA) or mild hypokalemia

PATIENTS AND METHODS

For the purposes of this retrospective study, medical data of 148 patients, hospitalized due to hypertension at the University Children's Hospital in Belgrade between January 2014 and October 2022 were obtained and processed. After establishing the diagnosis of AH, according to accepted recommendations (1), a general and targeted clinical examination and laboratory workup of importance for secondary causes of AH, and renal Doppler ultrasound, were performed, all according to the protocol for examining children with AH (7).

In patients with highly suspected RVH, DSA was performed. After giving detailed information and obtaining a written consent, DSA was performed by puncturing the femoral artery using the Seldinger technique. All procedures were done under medical sedation and local anes-

thesia, with antibiotic prophylaxis for bacterial endocarditis. Having punctured the femoral artery and placed he introducer sheath, a suitable tail catheter was introduced using a guide wire. A catheter with a wire was placed in the abdominal aorta at the place of origin of the renal artery. We used the low-osmolar contrast agent (Ultravist), with prior adequate intravenous hydration of the patient.

MRA was performed for diagnostic purposes in patients in whom secondary causes of hypertension were excluded after initial examination, but who had no adequate response to antihypertensive therapy, according to the protocol. After MRA, DSA was performed in patients with visible RBV stenosis and in patients with high clinical suspicion of RVH, in addition to a normal MRA finding. Also, MRA was done as a control imaging method, after therapeutic revascularization in patients with RVH (autotransplantation, balloon dilatation or stent placement). All MR examinations were performed on a 1.5 T whole-body MRI scanner (Magnetom Aera, Siemens AG, Healthcare Sector, Erlangen, Germany). Gadolinium-based contrast agent was used in the amount of 0.1 ml/kg of body weight.

The data were processed using descriptive statistical methods. For categorical data variables, the number (n) and percentage (%) were calculated.

RESULTS

After the initial tests (clinical examination, laboratory workup and renal Doppler ultrasound), due to a high suspicion of RVH, DSA was performed in 29 out of 148 patients included in the study. In 13 (45%) out of 29 patients, the diagnosis of RVH i.e., RBV stenosis was confirmed. The remaining 16 (55%) patients had normal findings on DSA **(Figure 1)**.

MRA was performed in 119 patients, and in 116 (97.5%) patients it was done in diagnostic purposes, whereas it was performed as a control imaging method after therapeutic revascularization in 3 (2.5%) patients. In 4 (3.5%) out of 116 diagnostic MRA, the result indicated RBV stenosis, and in 44 (38%) patients it indicated some other abnormality of the kidney parenchyma and the urinary tract or a variety of kidney blood vessels **(Figure 2)**.

Out of the 44 patients with some abnormality/variety on MRA, 25 (57%) had a variety of the RBV, 15 (34%) had some change in the kidney parenchyma, and 4 (9%) had an abnormality of lower parts of the urinary tract **(Figures 3 and 4)**.

After diagnostic MRA, DSA was performed in 7 (6%) out of 116 patients. In 4 patients it was done due to RVB stenosis observed on MRA, and in 3 patients it was performed due to high clinical suspicion of RVH despite MRA which did not confirm renal artery stenosis, but indicated some of the varieties of RBV **(Figure 5)**. In all 7 patients, DSA findings were normal.

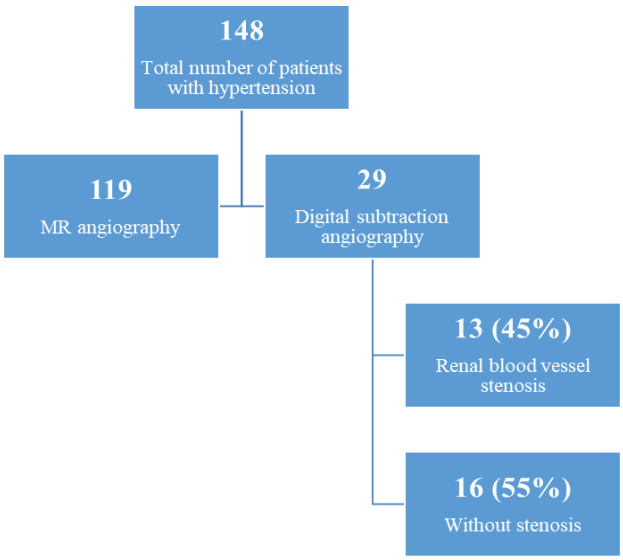


Figure 1. MR angiography and digital subtraction angiography (DSA) in patients with hypertension

DISCUSSION

Poorly controlled AH in childhood is one of the strongest predictors of AH in adulthood and its severe sequelae (myocardial infarction, stroke, encephalopathy) (15). Therefore, it is extremely important to diagnose AH in children, find its cause and provide an adequate treatment. RVH occurs as a result of reduced blood flow through one or both renal arteries due to their narrowing, which results in the activation of the renin-angiotensin-aldosterone system (16). Increased blood pressure is a compensatory mechanism that enables blood flow through a narrowed RBV, but over time it also leads to the damage of the target organ.

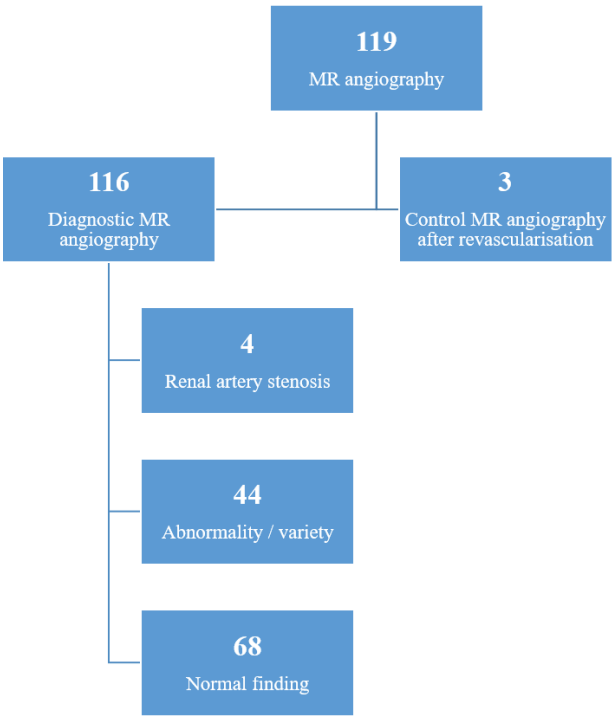


Figure 2. MR angiography in patients with hypertension

Other abnormalities (4)
Neurogenic bladder (2)
Ureter fissus (2)
Parenchyma abnormalities (15)
Cystic changes (11) • Solitary cyst (5) • Multiple cysts (6)
Scarring (2)
Agenesia, hypoplasia, dysplasia (2)

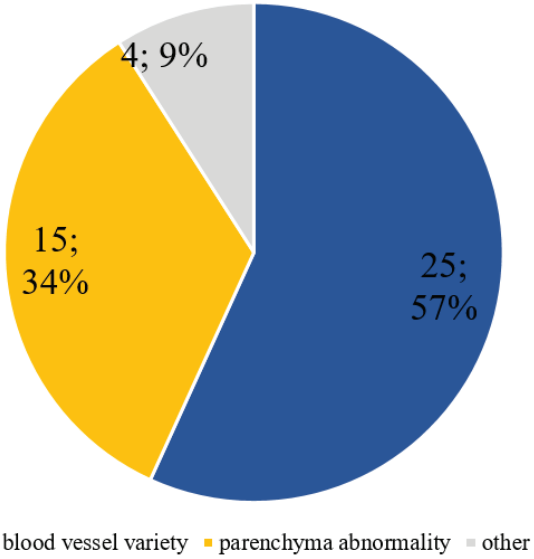
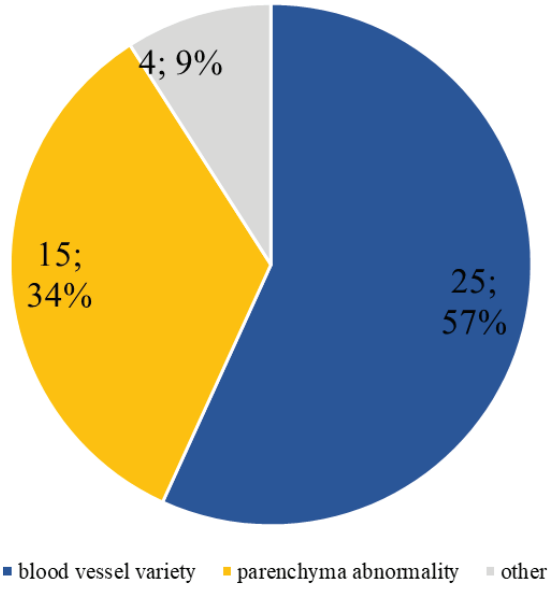


Figure 3. Parenchyma and other abnormalities in MR angiography findings

Considering all the specificities of the pediatric population, the clinical course, causes and outcomes of RVH compared to the adult population, the ideal imaging method in the diagnostic algorithm of RVH is still controversial (17). Although a relatively rare cause of secondary AH in children, RVH at this age has great possibilities of being treated with drug therapy, endovascular or surgical procedures (5, 13, 18). Therefore, the sensitivity of non-invasive diagnostic methods must be high, so that children with RVH do not remain undiagnosed and inadequately treated. Some authors consider non-invasive diagnostic methods as adequate screening for RVH (10-12, 16, 19). Results of other studies indicate poor sensitivity of these methods to exclude RBV stenosis, especially in case of intrarenal blood vessel stenosis, therefore it is recommended that DSA should be performed in all patients with high clinical suspicion of RBV stenosis, even when the results of non-invasive diagnostic methods are normal (9, 20-22). For now, according to the latest data from literature, non-invasive diagnostic methods, renal Doppler ultrasound, CTA and MRA cannot replace DSA, which is currently considered the most reliable diagnostic method for confirming RVH in children (6, 9, 17). The advantages of this method are certainly the best view of the lumen of the RBV, as well as the possibility of a therapeutic endovascular intervention (balloon dilation, stent placement) during the same procedure (9), as well as taking blood from the renal vein in order to measure local renin synthesis in unreliable DSA findings (23). However, it has been shown that the selective collection of venous blood from the renal veins, taken for determining plasma renin activity, as a method for diagnosing RVH has low sensitivity (74%) and specificity (59%), which is why it is not frequently used (6). According to American proto-



Renal artery varieties (25)
Two renal arteries for each kidney (3)
Two renal arteries for left kidney (9)
Two renal arteries for right kidney (5)
Artery diameter difference (3)
Aberrant left renal artery (1)
Gracile accessory branch of right renal artery (1)
Coiling (2)
Early branching of left renal artery (1)

Figure 4. Renal blood vessel varieties in MR angiography findings

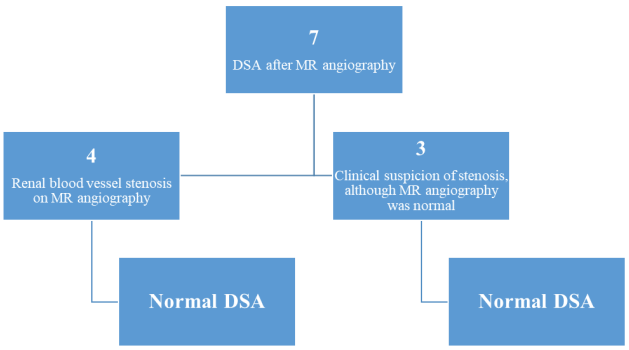


Figure 5. Digital subtraction angiography (DSA) after MR angiography

cols for adult patients with AH, blood sampling from renal veins is no longer recommended as a diagnostic method for detecting renal artery stenosis (24). Disadvantages of DSA are radiation to which children are exposed, the risk of arterial blood vessel injury and obtaining only indirect information about the blood vessel wall, which is important only from an etiological point of view (7, 22). According to the valid European and American guidelines for examining pediatric patients with AH (6, 7), it is recommended that patients with suspected RVH, after clinical and laboratory workup along with renal Doppler ultrasound, as the only non-invasive imaging method, should undergo the invasive DSA to definitively confirm the diagnosis. In children under 10 years of age, the procedure usually requires general anesthesia, while in older patients it is possible to apply local anesthesia (14). When carefully selecting patients, according to data from literature, 40-78% of DSA findings in this population indicate RBV stenosis (9, 25, 26). Our results are consistent with data from literature. In 29 out of 148 patients included in the study due to high suspicion of RVH, after the initial clinical, laboratory examination and renal Doppler ultrasound, DSA was performed. DSA findings confirmed RBV stenosis in 13/29 patients (45%).

The results of MRA in patients with suspected RVH are becoming increasingly more informative over time, and therefore the technical capabilities of MRA device are getting better, which facilitates the interpretation of findings by radiologists (14). A meta-analysis that included 998 adult patients from 25 studies indicated MRA sensitivity of 94% and specificity of 85% (27) for diagnosing the cause of RVH. The use of gadolinium as a contrast agent increased the sensitivity (97%) and specificity (93%) of the method (27-32). A study involving pediatric patients with suspected RVH indicated a lower sensitivity (80%) and specificity (63%) of MRA (9). In this study, MRA was performed in 39 patients, and stenosis of renal blood vessels, later confirmed by DSA, was not diagnosed in 10 patients (6 – main trunk of the renal artery, 2 – main branch of the renal artery, 2 – segmental

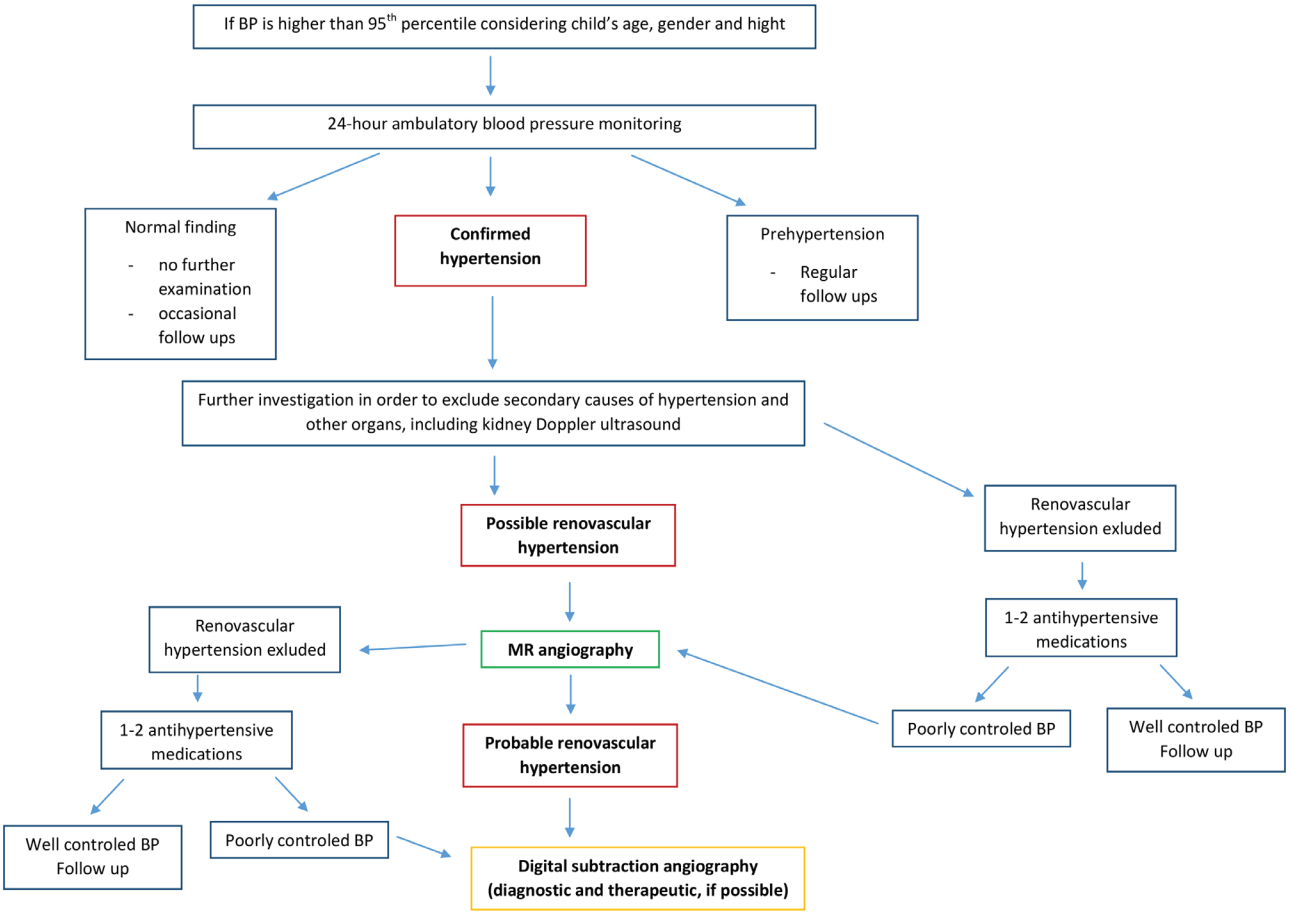


Figure 6. Recommended protocol for children with arterial hypertension

arteries). False positive results were observed in children with varieties of renal blood vessels (two renal arteries on one side, one of which is gracile but without stenosis on DSA). The authors state that the disadvantage of this study is that it is retrospective and includes patients from many centers around the world, where numerous radiologists worked on technically different devices and interpreted the results of the MRA scans. Louis et al. indicated an extremely low sensitivity (62.5%) and high specificity (100%) of MRA in 25 pediatric patients with fibromuscular dysplasia (19). Out of the 116 diagnostic MRA examinations performed in our patients, the results of the findings indicated suspected RBV stenosis in 4 patients, and some varieties of RBV in 25 patients. In 3 patients, we performed MRA as a control imaging method after DSA and one of the applied methods of revascularization of the stenotic RBV, which is why we intended to avoid an invasive imaging method and re-exposing the patient to radiation. The result of the control MRA was normal in all three patients. As the guidelines for pediatric patients with AH state (6, 7) in 7 patients we performed DSA after the diagnostic MRA, in 4 patients we performed it due to suspected RBV stenosis, and in 3 due to high clinical suspicion of RVH despite the fact that MRA did not indicate stenosis of the renal blood vessel, but some variety of kidney blood vessels. In all 7 patients, the DSA result did not indicate RBV stenosis. MRA has its importance in the diagnosis of RVH, but there are possible false positive or negative findings. MRA finding should always be defined in accordance with the clinical features and is part of the diagnostic workup in children with suspicious RVH.

It should not be forgotten that the most common cause, responsible for 60% of secondary hypertension in the pediatric patient population, is of renal parenchymal origin (glomerular diseases, renal parenchymal scars) (6) and that MRA images ideally show the renal parenchyma, so they represent an excellent non-invasive method for its evaluation (9). In 15/116 patients included in our study who underwent diagnostic MRA, changes in the kidney parenchyma were found. The most common ones were cystic changes in 11 patients, renal scarring in two patients and morphological changes such as agenesia/hypoplasia/dysplasia in two patients.

There is a small number of studies in pediatric population available in literature, which deal with the importance of this non-invasive diagnostic method. The reason for this are the specificities of the pediatric population, primarily in terms of the size of blood vessels, technical artifacts during MRA due to movement, small number of patients per center with technically different capabilities of the MRA device and a large number of radiologists who interpret the findings. Therefore, our opinion is that, despite the mentioned advantages of MRA, this non-invasive diagnostic method that does not require radiation has been insufficiently investigated and used in the pediatric population of patients with AH.

Current guidelines for examining pediatric patients with AH (6, 7) clearly state that after clinical and laboratory tests along with renal Doppler ultrasound, as the only initial non-invasive diagnostic method, when RVH is suspected, the patient should be referred directly to DSA in order to confirm the diagnosis. According to the data available in literature (9, 25, 26), and according to the results of our study, an average of about 50% of pediatric patients sent to DSA, due to highly suspicious RVH, had a normal finding. Therefore, in our opinion, it is justified to first refer pediatric patients with suspected RVH who are examined according to the above-mentioned guidelines, to MRA **(Figure 6)**. This way, a number of patients with a normal MRA finding would probably avoid DSA as an invasive diagnostic method that requires radiation and carries the already mentioned intervention risks. Certainly, patients with clinically highly suspected RVH, in the first place, and with an unsatisfactory response to two or more antihypertensive drugs, despite the normal findings of MRA, are justified to be referred to DSA. Also, over time, this way, we would have enough patients with highly suspicious RVH and performed MRA to adequately assess the sensitivity and specificity of this non-invasive diagnostic method in terms of diagnosing stenosis of the RBV.

CONCLUSION

We have presented our experience of using MRA in children with AH. RVH is an important cause of secondary AH in children and adolescents, and it requires a serious multidisciplinary approach by nephrologists, interventional radiologists/cardiologists and vascular surgeons. A clearer prediction of the diagnostic significance of the sensitivity and specificity of MRA in children with suspected RVH would be obtained by planning a prospective study under the same clinical, laboratory and technical conditions. Certainly, a great problem is the relatively small number of pediatric patients with suspected RVH per center, which is why multicenter studies are necessary to contribute to solving this problem.

Acknowledgments

None.

Conflict of interest

None to declare.

Authors' contributions

Study design: MC, MK. Acquisition: MC, GML, DP, BS, MĐ, PP, IG, TR, IS. Analysis: MC, MK, AP, TG. Data interpretation: MC, MK, AP. Preparing the draft version of

the manuscript: MC, MK, AP. Revising the manuscript: MC, MK, AP, GML, DP, BS, MĐ, PP, IG, TG, TR, IS.

Ethical approval

This research and publication were approved by the Ethical committee of the University Children's Hospital (approval number 017 16/2).

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PRIMENA MAGNETNE ANGIOGRAFIJE KOD DECE SA ARTERIJSKOM HIPERTENZIJOM - ISKUSTVO JEDNOG CENTRA

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Sažetak

Uvod: Stenoza renalnog krvnog suda (RKS) uzrok je sekundarne arterijske hipertenzije (AH) kod 10% dece. Digitalna subtrakciona angiografija (DSA) je zlatni standard za postavljanje dijagnoze stenoze RKS. Mnogi autori razmatraju MR angiografiju (MRA) kao adekvatnu neinvaznu dijagnostičku metodu koja ne zahteva zračenje. Cilj ovog rada je analiza iskustva našeg centra u primeni MRA kod dece sa AH.

Metod: U ovu retrospektivnu studiju uključeno je 148 pacijenata hospitalizovanih na Univerzitetskoj dečjoj klinici u Beogradu, zbog AH. Nakon inicijalnih ispitivanja, pacijentima je učinjena DSA i/ili MRA.

Rezultati: Prema važećim smernicama kod 29/148 pacijenata zbog visoke sumnje na stenozu RKS učinjena je DSA i dijagnoza je potvrđena kod 13/29 (45%). Dijagnostička MRA je učinjena kod 116/119 (97,5%), a kao kontrolna, nakon terapijske revaskularzijacije kod 3/119 (2,5%) pacijenata. Kod 4/116 (3,5%) nalaz je ukazao na stenozu RKS, a kod 44/116 (38%) pacijenata na neku drugu abnormalnost parenhima bubrega i urinarnog trakta ili varijetet RKS. Posle MRA, DSA je urađena kod 7/116 (6%) pacijenata (4 sa nalazom stenoze RKS na MRA, 3 sa kliničkom sumnjom na stenozu RKS i urednim nalazom MRA). Rezultat je bio uredan kod svih.

Zaključak: Prema našim rezultatima, opravdano je deci sa visokosuspektnom stenozom RKS, pre DSA, uraditi dijagnostičku MRA, kako bi se kod jednog broja pacijenata sa urednim nalazom izbegla DSA, kao invazivna procedura sa zračenjem. Pored toga vremenom bismo imali jasniji uvid u senzitivnost i specifičnost MRA kao dijagnostičke metode za stenozu RKS kod dece.

Ključne reči: Stenoza renalnog krvnog suda, arterijska hipertenzija, MR angografija, digitalna subtrakciona angiografija, deca

Primljen: 30.01.2023. I **Revizija:** 02.03.2023. I **Objavljen:** 20.04. 2023

Medicinska istaživanja 2023; 56(2):61-68